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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/768,742	TERPETSCHNIG ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-30,33,37-41,83,88 and 89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-30,33,37-41,83,88 and 89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 83, 28-30, 37-41, 88 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laing et al., 6,331,392, in view of Sportsman et al., 6,806,053.

As to independent claim 83, Laing et al. discuss fluorescence polarization and disclose that the degree to which the fluorescence emission vector moves is directly related to the mobility of the fluorescently labeled molecule. If the fluorescently labeled molecules are large, they move very little and the emitted light remains highly polarized with respect to the excitation plane. In contrast if the fluorescently labeled molecules are small, they rotate or tumble faster, and the resulting emitted light is depolarized relative to the excitation plane (col. 8, lines 45-54.) Moreover, Laing et al. teach in an embodiment, an RNA target conjugated to a larger molecule, such as streptavidin for binding to a biotin moiety attached to the target RNA, thereby enhancing differences in polarization of the fluorescent probe subsequent to ligand binding (col. 9, lines 44-50).

However, in this embodiment, Laing et al. do not disclose using a bead complex (e.g., streptavidin-bead conjugate) as an alternative to the streptavidin alone, as a means for enhancing differences in polarization subsequent to binding.

Sportsman et al. however teach that the change in polarization upon binding can be increased by decreasing the mobility of the binding partner for the labeled species. Mobility can be decreased by increasing the size of the binding partner either directly or by forming a complex with a mass label. Suitable mass labels include other molecules and beads among others. Attachment to other molecules, beads, and/or surfaces may be accomplished using any of a number of well-known reactive groups (col. 21, lines 14-55.)

In short, both Laing et al. and Sportsman et al. teach that there is a correlation between size of the complex to be detected and the detected polarization, with Laing et al. teaching attachment of a target to a larger molecule to enhance the difference in polarization before and after ligand binding, and Sportsman et al. teaching increasing the size of the binding partner by forming a complex with a mass label such as other molecules or beads. Thus, Sportsman et al. teach that beads are alternatives to molecules for use as mass labels to enhance the difference in polarization before and after a reaction. It would have been obvious to the skilled artisan to utilize beads instead of molecules in the Laing et al. invention as the means to increase the polarization difference before and after a reaction because Sportsman et al. teach that beads are alternatives to molecules since they provide the same function of increasing the size of a complex to increase the polarization difference.

Moreover, while neither Laing et al. nor Sportsman et al. teach mass labeling the *product* as opposed to either initial reagent (Laing et al. teach attaching the large molecule, which is essentially a mass label, to the target, and fluorescently labeling the probe; and Sportsman et al. teach mass labeling the binding partner for the labeled species), the skilled artisan however would recognize that in both cases, the fluorescently labeled complex increases in size upon formation of the product from the reaction, which in turn enhances the difference in polarization before and after a reaction as discussed by both Laing et al. and Sportsman et al. Moreover, it is predictable by the skilled artisan that providing a mass label that binds only to the product and not to the initial reagents (e.g., an enzyme substrate) and fluorescently labeling the substrate also produces the same result of increasing the size of the labeled complex (e.g., the labeled substrate) to enhance the difference in polarization before and after a reaction, and such predictability renders the technique obvious. Also, performing an assay to detect the product of an enzyme-substrate reaction is known and desirable, as shown by Sportsman et al. (see for example, col. 8, lines 36-47) and thus, tailoring the technique discussed above to detect specifically a product of an enzyme-substrate reaction would also have been within the skills of the ordinary artisan. The fluorescent label discussed by Laing et al. is equivalent to Applicant's claimed luminophore and the beads discussed by Sportsman et al. is equivalent to Applicant's claimed mass label.

As to claim 28, the fluorescent label is inherently photoluminescent.

As to claim 29, neither Laing et al. nor Sportsman et al. teach that the additional limitations recited in claim 29. However, whether the photoluminescence lifetime is greater than the rotational correlation time of the unbound probe (luminophore) and less than the rotational correlation time of the complex formed by binding of the substrate to the mass label depends on what fluorescent moiety is used and what choice of enzymes and substrates are used. Moreover, the photoluminescence lifetime as claimed by Applicant appears to be an optimum or workable range. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art (see MPEP 2144.05 IIA, citing In re Aller, 105 USPQ 233.)

As to claim 30, Sportsman et al. teach that the luminophore may be coupled to the analyte covalently or noncovalently, such as by using specific binding pairs such as avidin and biotin, or protein A and immunoglobulins, or lectins and sugars (col. 11, lines 5-16). While this disclosure refers to attaching the luminophore to the analyte, the skilled artisan would recognize that these same techniques can be tailored to couple a luminophore to various molecules such as the substrate in the method discussed above regarding claim 83.

As to claim 37, the luminophore is not normally present in the sample. (The Office notes that this is a recitation of intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from

the prior art. If the prior art structure is capable of performing the intended use, such as in this case, then it meets the claim.)

As to claim 38, the mass label is not normally present in the sample (The Office notes that this is also a recitation of intended use, and the prior art structure is capable of performing the intended use.)

As to claim 39, the property of the luminophore is related to a rotational diffusion coefficient of the luminophore. It is noted that Applicant does not specify what property of the luminophore, therefore the claim encompasses any property of the luminophore, including its polarization.

As to claim 40, the property may be measured using polarization (see Laing et al.., col. 9, lines 44-50).

As to claim 41, the property of the luminophore is related to the translational diffusion coefficient of the luminophore. It is noted that Applicant does not specify what property of the luminophore, therefore the claim encompasses any property of the luminophore, including its polarization.

As to claim 88, the mass label (bead) is capable of binding specifically to the product (as discussed above regarding claim 83), and the luminescence property of the luminophore is different for the luminophore bound to the substrate than for a complex of the luminophore, the product, and the mass label (see Sportsman et al. col. 21, lines 14-55, and discussion of claim 83 above).

As to claim 89, the luminescence property may be measured using fluorescence polarization (see Sportsman et all, col. 21, lines 14-55 and discussion of claim 83 above.)

Claims 33-36 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laing et al., 6,331,392, in view of Sportsman et al., 6,806,053, as applied to independent claim 83 above, and further in view of Yguerabide et al., 6,586,193.

Laing et al. in view of Sportsman et al. disclose the invention substantially as claimed (see discussion of independent claim 83 above), except for the mass label comprising a plurality of binding moieties that are capable of binding to the products (as recited in claim 33), or the mass label being a first mass label and the method further comprising a second mass label that is capable of binding to the product or first mass label or a combination thereof but not the luminophore alone (as recited in claim 34).

However, Yguerabide et al. teach aggregating or cross-linking of beads produced by the presence of an analyte can be detected in polarization assays (col. 84, lines 26-41). Yguerabide et al. teach that these assays involve the association or aggregation of two or more particles by interaction of analyte and specifici analyte recognition reagents, and that it is known in the art that by using the appropriate binding agents and concentration of binding agents and analyte (for example an antigen that is multivalent), agglutination, aggregation, cross-linking, networking and similar binding events can occur and that these events can be used to detect one or more analytes in a sample.

Yguerabide et al. disclose that for example visible precipitates are formed if the antigen is soluble and multivalent (col. 83, lines 53-59. Moreover, Yguerabide et al. teach that the disclosed invention allows for easier use, more sensitive and versatile detection of analytes and that the type of aggregates formed depends on the size of the cross-linking agents and their valency and the type of binding agent attached to the particle (col. 84, lines 1-11.) The skilled artisan would thus recognize that using multiple probes on a bead and/or probes for a multivalent analyte in the invention of Laing et al. as modified by Sportsman et al. will produce such cross-linking as disclosed by Yguerabide. The skilled artisan would have been motivated to provide for such cross-linking in the Laing et al.-Sportsman et al. invention because Yguerabide et al. teach that this allows for the advantages of easier use, more sensitive and versatile detection of analytes.

As to claim 35, Yguerabide et al. disclose that aggregates formed can comprise two particles to many (col. 84, line 11) (see also for example col. 88, lines 3-12). Thus Yguerabide et al. disclose a network of for example three mass labels (a second mass label bound to two first mass labels, as recited by Applicants

As to claim 36, Yguerabide et al. teach that the second mass label includes at least biotin (col. 88, lines 3-12). (The Office notes that although Yguerabide et al. teach that the second mass label includes biotin indirectly, through linkage with streptavidin, the claim nevertheless read on this disclosure.)

As to claim 84, Sportsman et al. does not disclose the material of the beads, more specifically, that they are made of glass. However, Yguerabide et al. disclose that

beads of various materials may be used, such as glass beads. Thus using beads comprising glass in the Laing et al.-Sportsman et al. invention would have been within the skills of the ordinary artisan as Yguerabide et al. disclose such materials for use as assay beads.

Response to Arguments

Applicant's response has been considered. Applicant asserts that Examiner had not addressed the limitation regarding the mass label binding to the product but not capable of binding to the substrate. Examiner had pointed to the fragment that is not attached to the bead as being the substrate, which upon reconsideration, is not reasonable as it is actually a part of product of the enzymatic reaction. New grounds for rejection has been made however, under Laing et al. and Sportsman et al. The present Office action is made nonfinal to give Applicants an opportunity to respond.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ann Y. Lam
Primary Patent Examiner